

AMENDMENTS TO THE DRAWINGS

Please replace Figure 13 with the Replacement Sheet for Figure 13.

Please replace Figure 21B with the Replacement Sheet for Figure 21B.

REMARKS

1. Formal Matters

a. Status of the Claims

Claims 1-22 are pending in this application. Claims 1-22 are hereby canceled without prejudice to pursuing these claims in a continuing application. Claims 23-34 are new. Upon entry of these amendments, claims 23-34 are pending and under active consideration. Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application.

b. Amendments to the Claims

New claim 23 recites a nucleic acid consisting of 19 to 140 nucleotides, support for which may be found throughout the application including paragraph 0049 and 0050 of the application as originally filed. New claim 23 also recites that the sequence of the nucleic acid may comprise at least 19 consecutive nucleotides of SEQ ID NO: 4204050, support for which may be found at Table_2_B, lines 4474648-4474741 and 4617066-4617159 of the application as originally filed.

Claim 23 is also amended to recite that the nucleic acid may be an RNA equivalent of (a), support for which may be found in the application as originally filed including at paragraph 0201 and Table_2_B, lines 4474648-4474741 and 4617066-4617159 of the application as originally filed.

Claim 23 is also amended to recite that the nucleic acid may be: a sequence at least 52/67 identical to (a) or (b), support for which may be found at Table_4, lines 608189-608192 as originally filed. SEQ ID NO: 4204050 forms a hairpin, as shown at Table_4, lines 608189-608192 of the application as originally filed. SEQ ID NO: 4204050 is 67 nucleotides in length. Within the predicted hairpin formed by SEQ ID NO: 4204050, 52 complementary nucleotides are paired.

Claim 23 is also amended to recite that the nucleic acid may be: the complement of any one of (a)-(c), support for which may be found at Table_2_B, lines 4474648-4474741 and 4617066-4617159 of the application as originally filed.

New claim 24 recites the nucleic acid of claim 23, wherein the at least 19 nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 117937 and 118171, support

for which can be found at Table_1, lines 117941, 241237, 241917, and 241919 of the application as originally filed.

New claim 25 recites a nucleic acid of claim 23, wherein the nucleic acid consists of 19 to 24 nucleotides, support for which can be found at paragraph 0050 of the application as originally filed.

New claim 26 recites a nucleic acid with a sequence consisting of (a) at least 19 consecutive nucleotides of SEQ ID NO: 4204050; (b) an RNA equivalent of (a); (c) a sequence at least 52/67 identical to (a) or (b); or (d) the complement of any one of (a)-(c), support for which may be found as described above for new claim 23.

New claim 27 recites a nucleic acid of claim 26, wherein the at least 19 nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 117937 and 118171, support for which can be found as described for new claim 24.

New claim 28 recites a nucleic acid of claim 26, wherein the nucleic acid consists of 19 to 24 nucleotides, support for which can be found as described for new claim 25.

New claim 29 recites a nucleic acid of claim 24, wherein the nucleic acid is an RNA, support for which can be found at paragraph 0201 and Table_2_B, lines 4474648-4474741 and 4617066-4617159 of the application as originally filed.

New claim 30 recites a nucleic acid of claim 27 wherein the nucleic acid is an RNA, support for which can be found at paragraph 0201 and Table_2_B, lines 4474648-4474741 and 4617066-4617159 of the application as originally filed.

New claim 31 recites a vector comprising an insert, wherein an insert consists of the nucleic acid of claim 23, support for which can be found at paragraph 0035 of the application as filed.

New claim 32 recites a vector comprising an insert, wherein an insert consists of the nucleic acid of claim 26, support for which can be found at paragraph 0035 of the application as filed.

New claim 33 recites a probe comprising an insert, wherein an insert consists of the nucleic acid of claim 23, support for which can be found at paragraph 0035 of the application as originally filed.

New claim 34 recites a probe comprising an insert, wherein an insert consists of the nucleic acid of claim 26, support for which can be found at paragraph 0035 of the application as originally filed.

c. Amendments to the Specification

Paragraph 0181 of the Brief Description of the Drawings is amended to assign SEQ ID NOS: 4205040-4205050 to the sequences shown in Fig. 14B in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0183 of the Brief Description of the Drawings is amended to assign SEQ ID NOS: 4205035-4205039 to the sequences shown in Fig. 15A in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0192 of the Brief Description of the Drawings is amended to assign SEQ ID NOS: 4205083-4205093 to the sequences shown in Fig. 19 in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0345 is amended to assign SEQ ID NOS: 4204916-4204920 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraphs 0360-0362 are amended to assign SEQ ID NOS: 4204921-4204926 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0364 is amended to assign SEQ ID NOS: 4204927-4204928 and 4204947 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0389 is amended to assign SEQ ID NOS: 4204929-4204934 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0392 is amended to assign SEQ ID NOS: 4204935-4204936 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraphs 0453-0473 are amended to assign SEQ ID NOS: 4204937-4204946 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

d. Amendments to the Drawings

Figure 13 is amended by replacing it with a Replacement Sheet for Fig. 13 to assign SEQ ID NOS: 4204948-4205034 and 4205094-4205095 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Figure 21B is amended by replacing it with a Replacement Sheet for Fig. 21B to assign SEQ ID NOS: 4205051-4205082 to the listed sequences in compliance with 37 C.F.R. §§1.821-1.825. No new matter has been added.

e. Notice to Comply with Sequence Rules

On page 2 of the Office Action, the Examiner alleges that the specification and sequence listing do not comply with 37 C.F.R. §§ 1.821-1.825. Specifically, the Examiner alleges that SEQ ID NOS are not associated with sequences disclosed in Figures 13, 14B, 15A, 19A, 19D, 19E, and 21B, and paragraphs 0345, 0360-0362, 0364, 0389, 0392, and 0453-0473.

Applicant submits herewith a replacement sequence listing pursuant to 37 C.F.R. § 1.825(a), and the specification and drawings are amended throughout to disclose the appropriate SEQ ID NOS in accordance with 37 C.F.R. §§ 1.821-1.825. No new matter has been added.

With regard to the Examiner's comments in connection with paragraph 0123 and Figures 21A, 22A, 23A, Applicant respectfully submits that the Examiner is in error. Applicant has concluded from careful review of the application that the aforementioned paragraph does not disclose sequences and that Figures 21A, 22A, and 23A are not associated with the instant application. In light of the amendments to the specification described hereinabove and the replacement sequence listing submitted herewith, Applicant respectfully submits that the application is in compliance with 37 C.F.R. §§ 1.821-1.825.

f. Election/Restrictions

On pages 3-8 of the Office Action, the Examiner requires restriction to one of the following inventions under 35 U.S.C. § 121:

- I. Claims 1-9 and 18-22, drawn to a bioinformatically detectable oligonucleotide.
- II. Claims 10-15, drawn to a method of treatment of a disease by modulating the activity of a microRNA that binds to a segment of mRNA that pathogenically expresses a protein.
- III. Claim 16, drawn to a method of diagnosis of a disease using a microRNA to bind a mRNA encoding a protein that is abnormally expressed.
- IV. Claim 17, drawn to a method for detection of expression of an oligonucleotide.

Applicant elects without traverse Group I, which now is considered claims 23-34, drawn to an isolated nucleic acid, a vector comprising said nucleic acid, a probe comprising said nucleic

acid, a gene expression inhibition system comprising said vector, and a means for inserting said vector into a cell.

g. Sequence Election for All Groups

On page 8 of the Office Action, the Examiner further requires election of a single nucleic acid sequence for the elected Group I under 35 U.S.C. § 121.

Applicant elects with traverse nucleic acids related to SEQ ID NO: 4204050, which is associated with claims 23-34.

The Examiner is permitted under 35 U.S.C. § 121 to issue a restriction requirement between independent and distinct inventions. However, the Director has partially waived the requirements of 37 C.F.R. § 1.141 *et seq.* to permit a reasonable number of nucleotide sequences to be claimed in a single application. *See Examination of Patent Applications Containing Nucleotide Sequence*, 1192 O.G. 68 (November 19, 1996). It has been determined that normally **ten** sequences constitute a reasonable number for examination purposes absent an exceptional case. *See* MPEP 803.04.

The Examiner has failed to demonstrate that the claimed sequences are an exceptional case necessitating that the number of sequences to be selected be less than ten. Applicant respectfully submits that the Examiner is impermissibly disregarding the waiver of 37 C.F.R. § 1.141 *et seq.* Accordingly, Applicant respectfully requests reconsideration of the restriction requirement and the opportunity to elect up to ten sequences for further prosecution.

2. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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